

CLAIMS

1. A compound which is:

5 3-Amino-*N*-(3-nitrophenyl)-6-[4-(pyrrolidin-1-ylsulfonyl)phenyl]pyrazine-2-carboxamide;

3-Amino-6-[4-(pyrrolidin-1-ylsulfonyl)phenyl]-*N*-1*H*-tetrazol-5-ylpyrazine-2-carboxamide;

10 *N*-[3-(Acetylamino)phenyl]-3-amino-6-[4-[(4-methyl-1-piperazinyl)sulfonyl]phenyl]-2-pyrazinecarboxamide;

3-Amino-*N*-[3-(aminosulfonyl)phenyl]-6-[4-[(4-methyl-1-piperazinyl)sulfonyl]phenyl]-2-pyrazinecarboxamide;

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as a free base or a pharmaceutically acceptable salt, solvate or solvate of a salt thereof;

3-Amino-6-[4-({[(1*R*)-2-methoxy-1-methylethyl]amino}sulfonyl)phenyl]-*N*-pyridin-3-ylpyrazine-2-carboxamide hydrochloride;

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3-Amino-6-[4-({[(1*S*)-2-methoxy-1-methylethyl]amino}sulfonyl)phenyl]-*N*-pyridin-3-ylpyrazine-2-carboxamide hydrochloride;

25 3-Amino-6-(4-{{[(2-ethoxyethyl)amino]sulfonyl}phenyl})-*N*-pyridin-3-ylpyrazine-2-carboxamide hydrochloride;

3-Amino-*N*-(2-methoxyphenyl)-6-{4-[(4-methylpiperazin-1-yl)sulfonyl]phenyl}pyrazine-2-carboxamide hydrochloride;

30 3-Amino-*N*-(4-methoxyphenyl)-6-{4-[(4-methylpiperazin-1-yl)sulfonyl]phenyl}pyrazine-2-carboxamide hydrochloride;

3-Amino-*N*-[2-(aminocarbonyl)phenyl]-6-{4-[(4-methylpiperazin-1-yl)sulfonyl]phenyl}pyrazine-2-carboxamide hydrochloride;

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3-Amino-*N*-[3-(aminocarbonyl)phenyl]-6-{4-[(4-methylpiperazin-1-yl)sulfonyl]phenyl}pyrazine-2-carboxamide hydrochloride;

40 3-Amino-*N*-(3-cyanophenyl)-6-{4-[(4-methylpiperazin-1-yl)sulfonyl]phenyl}pyrazine-2-carboxamide hydrochloride;

3-Amino-*N*-(2-bromophenyl)-6-{4-[(4-methylpiperazin-1-yl)sulfonyl]phenyl}pyrazine-2-carboxamide hydrochloride;

3-Amino-*N*-(3-bromophenyl)-6-{4-[(4-methylpiperazin-1-yl)sulfonyl]phenyl}pyrazine-2-carboxamide hydrochloride;

5 3-Amino-6-{4-[(4-methylpiperazin-1-yl)sulfonyl]phenyl}-*N*-1*H*-pyrazol-3-ylpyrazine-2-carboxamide hydrochloride;

3-Amino-*N*-[4-(aminocarbonyl)-1*H*-pyrazol-3-yl]-6-{4-[(4-methylpiperazin-1-yl)sulfonyl]phenyl}pyrazine-2-carboxamide hydrochloride;

10 3-Amino-*N*-1*H*-imidazol-2-yl-6-{4-[(4-methylpiperazin-1-yl)sulfonyl]phenyl}pyrazine-2-carboxamide hydrochloride;

3-amino-6-[3-fluoro-4-[2-(4-morpholinyl)ethoxy]phenyl]-*N*-3-pyridinyl-2-pyrazinecarboxamide hydrochloride;

15 3-Amino-6-[4-[[[(1-ethyl-3-piperidinyl)amino]sulfonyl]phenyl]-*N*-3-pyridinyl-2-pyrazinecarboxamide hydrochloride;

20 3-Amino-6-[4-[[bis(2-methoxyethyl)amino]sulfonyl]phenyl]-*N*-3-pyridinyl-2-pyrazinecarboxamide hydrochloride;

3-Amino-6-[4-[[[(3-methylbutyl)amino]sulfonyl]phenyl]-*N*-3-pyridinyl-2-pyrazinecarboxamide hydrochloride;

25 3-Amino-6-[4-[[[(1*S*)-2-methoxy-1-methylethyl]amino]carbonyl]phenyl]-*N*-3-pyridinyl-2-pyrazinecarboxamide hydrochloride;

3-Amino-*N*-3-pyridinyl-6-[4-[[[2-(1-pyrrolidinyl)ethyl]amino]carbonyl]phenyl]-2-pyrazinecarboxamide hydrochloride;

30 3-Amino-*N*-(3-methoxyphenyl)-6-[4-[(4-methyl-1-piperazinyl)sulfonyl]phenyl]-2-pyrazinecarboxamide hydrochloride;

35 *N*-(3-Acetylphenyl)-3-amino-6-[4-[(4-methyl-1-piperazinyl)sulfonyl]phenyl]-2-pyrazinecarboxamide hydrochloride;

3-Amino-6-[4-[(4-methyl-1-piperazinyl)sulfonyl]phenyl]-*N*-[3-(trifluoromethyl)phenyl]-2-pyrazinecarboxamide hydrochloride;

40 or as a free base or an alternative pharmaceutically acceptable salt, solvate or solvate of a salt thereof.

2. A pharmaceutical formulation comprising as active ingredient a therapeutically effective amount of the compound according to claim 1 in association with pharmaceutically acceptable carriers or diluents.

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3. The pharmaceutical formulation according to claim 2 for use in the prevention and/or treatment of conditions associated with glycogen synthase kinase-3.
- 5 4. A compound as defined in claim 1 for use in therapy.
5. Use of a compound according to claim 1 in the manufacture of a medicament for prevention and/or treatment of conditions associated with glycogen synthase kinase-3.
- 10 6. Use of a compound according to claim 1 in the manufacture of a medicament for prevention and/or treatment of dementia, Alzheimer's Disease, Parkinson's Disease, Frontotemporal dementia Parkinson's Type, Parkinson dementia complex of Guam, HIV dementia, diseases with associated neurofibrillar tangle pathologies and dementia pugilistica.
- 15 7. The use according to claim 6 wherein the prevention and/or treatment is Alzheimer's Disease.
8. Use of a compound according to claim 1 in the manufacture of a medicament for
20 prevention and/or treatment of amyotrophic lateral sclerosis, corticobasal degeneration, Down syndrome, Huntington's Disease, postencephalatic parkinsonism, progressive supranuclear palsy, Pick's Disease, Niemann-Pick's Disease, stroke, head trauma and other chronic neurodegenerative diseases, Bipolar Disease, affective disorders, depression, schizophrenia, cognitive disorders, hair loss, contraceptive medication, Type I and Type II
25 diabetes, diabetic neuropathy and diabetes related disorders.
9. The use according to claim 8 wherein the prevention and/or treatment is Type I and Type II diabetes, diabetic neuropathy and diabetes related disorders.
- 30 10. Use of a compound according to claim 1 in the manufacture of a medicament for prevention and/or treatment of predemented states, Mild Cognitive Impairment, Age-Associated Memory Impairment, Age-Related Cognitive Decline, Cognitive Impairment

No Dementia, mild cognitive decline, mild neurocognitive decline, Late-Life Forgetfulness, memory impairment and cognitive impairment, vascular dementia, dementia with Lewy bodies, Frontotemporal dementia and androgenetic alopecia.

5 11. A method of prevention and/or treatment of conditions associated with glycogen synthase kinase-3, comprising administering to a mammal, including man in need of such prevention and/or treatment, a therapeutically effective amount of a compound defined in claim 1.

10 12. A method of prevention and/or treatment of dementia, Alzheimer's Disease, Parkinson's Disease, Frontotemporal dementia Parkinson's Type, Parkinson dementia complex of Guam, HIV dementia, diseases with associated neurofibrillar tangle pathologies and dementia pugilistica, comprising administering to a mammal, including man in need of such prevention and/or treatment, a therapeutically effective amount of a
15 compound defined in claim 1.

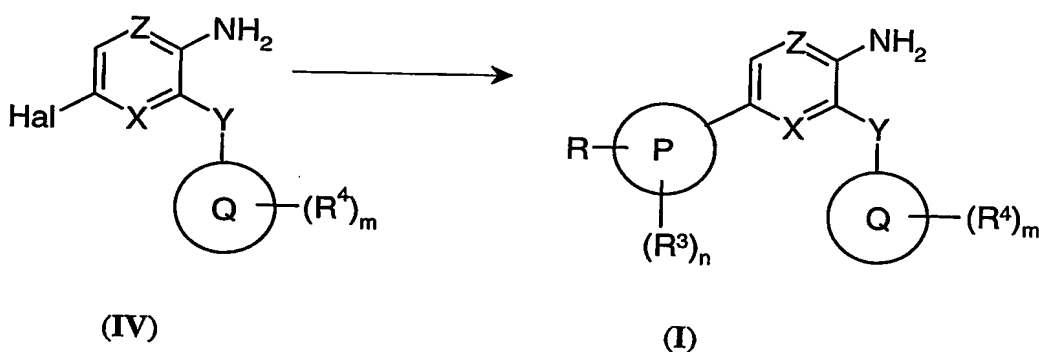
13. The method according to claim 12, wherein the prevention and/or treatment is Alzheimer's Disease.

20 14. A method of prevention and/or treatment of amyotrophic lateral sclerosis, corticobasal degeneration, Down syndrome, Huntington's Disease, postencephalatic parkinsonism, progressive supranuclear palsy, Pick's Disease, Niemann-Pick's Disease, stroke, head trauma and other chronic neurodegenerative diseases, Bipolar Disease, affective disorders, depression, schizophrenia, cognitive disorders, hair loss, contraceptive medication, Type I
25 and Type II diabetes, diabetic neuropathy and diabetes related disorders comprising administering to a mammal, including man in need of such prevention and/or treatment, a therapeutically effective amount of a compound defined in claim 1.

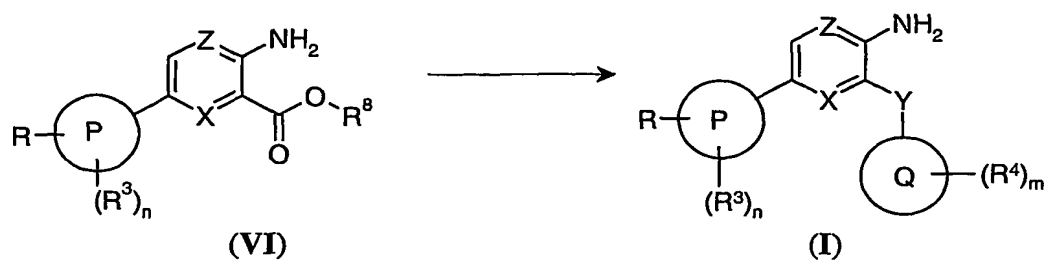
30 15. The method according to claim 14, wherein the prevention and/or treatment is Type I and Type II diabetes, diabetic neuropathy and diabetes related disorders.

16. A method of prevention and/or treatment of predemented states, Mild Cognitive Impairment, Age-Associated Memory Impairment, Age-Related Cognitive Decline, Cognitive Impairment No Dementia, mild cognitive decline, mild neurocognitive decline, Late-Life Forgetfulness, memory impairment and cognitive impairment, vascular dementia, dementia with Lewy bodies, Frontotemporal dementia and androgenetic alopecia, comprising administering to a mammal, including man in need of such prevention and/or treatment, a therapeutically effective amount of a compound defined in claim 1.
17. A process for the preparation of a compound defined in claim 1 which falls under the general formula I, wherein Y, X, Z, P, Q, R, R¹, R², R³, R⁴, R⁵, R⁶, R⁷, A, m and n are defined as in formula I, comprising of:

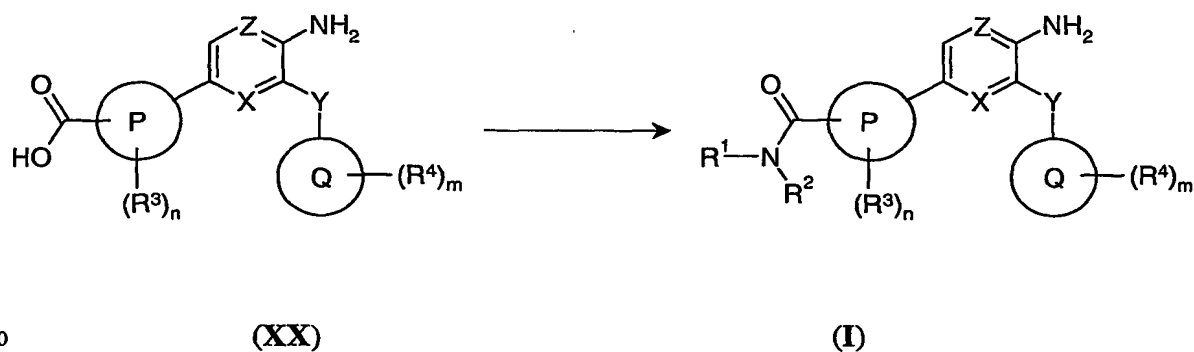
A) de-halogen coupling of a compound of formula IV where Hal is halogen with a appropriate aryl species to give a compound of formula I:



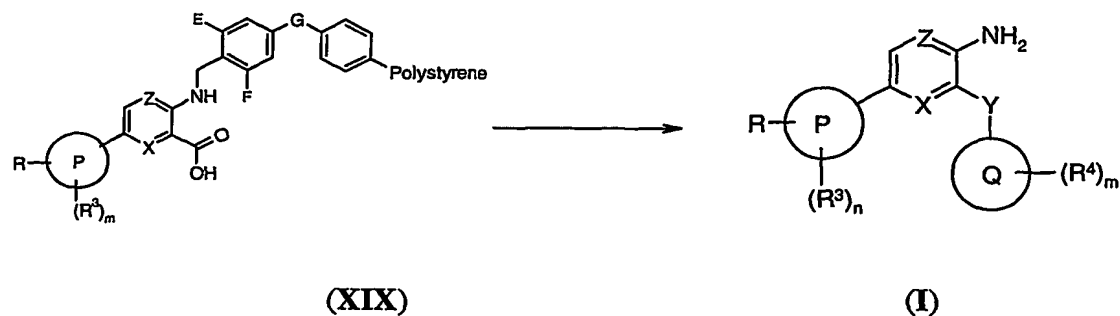
B) amidation of a compound of formula **VI** wherein R^8 is C_{1-6} alkyl or hydrogen with the appropriate amine:



C) amidation of a compound of formula **XX**, with the appropriate amine to give a compound of formula **I**:



D) amidation of a compound of formula **XIX** with the appropriate amine and treating with coupling reagents:



18. A compound which is 3-Amino-6-bromo-*N*-pyridin-3-ylpyrazine-2-carboxamide as a free base or a salt, solvate or solvate of a salt thereof.

5 19. A compound which is:

4-Bromo-*N*-[(1*R*)-2-hydroxy-1-methylethyl]benzenesulfonamide;

4-Bromo-*N*-[(1*R*)-2-methoxy-1-methylethyl]benzenesulfonamide;

10 4-Bromo-*N*-[(1*S*)-2-methoxy-1-methylethyl]benzenesulfonamide;

4-Bromo-*N*-(1-ethyl-3-piperidinyl)benzenesulfonamide;

4-Bromo-*N,N*-bis(2-methoxyethyl)benzenesulfonamide;

15 4-Bromo-*N*-(3-methylbutyl)-benzenesulfonamide;

4-Bromo-*N*-(2-ethoxyethyl)benzenesulfonamide;

as a free base or a salt, solvate or solvate of a salt thereof.

20 20. A compound which is:

Methyl 3-amino-6-[4-(pyrrolidin-1-ylsulfonyl)phenyl]pyrazine-2-carboxylate;

Methyl 3-amino-6-[4-[(4-methyl-1-piperazinyl)sulfonyl]phenyl]pyrazine-2-carboxylate;

25 3-Amino-6-[4-[(4-methyl-1-piperazinyl)sulfonyl]phenyl]-2-pyrazinecarboxylic acid;

as a free base or a salt, solvate or solvate of a salt thereof.

21. A compound which is:

4-[(4-Methylpiperazin-1-yl)sulfonyl]phenylboronic acid;

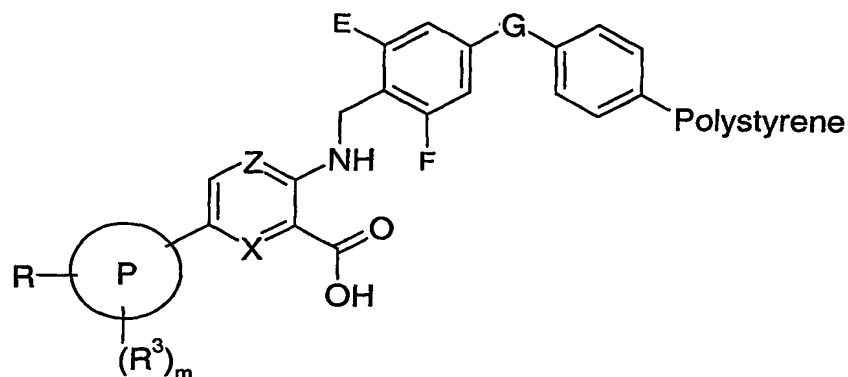
30 4-(Pyrrolidin-1-ylsulfonyl)phenylboronic acid;

as a free base or a salt, solvate or solvate of a salt thereof.

22. A compound which is:

4-[2-(4-Bromo-2-fluorophenoxy)ethyl]morpholine as a free base or a salt, solvate or solvate of a salt thereof.

23. A compound which is:



wherein R, R³, P, X, Z, and m are as defined above, and wherein E and F are a methoxy group or hydrogen and G is a spacer chain containing atoms selected from oxygen and carbon as a free base or a salt, solvate or solvate of a salt thereof.

24. A compound which is:

3-{[2,6-Dimethoxy-4-(2-phenylethoxy)benzyl]amino}-6-[4-(pyrrolidin-1-ylsulfonyl)phenyl]pyrazine-2-carboxylic acid polystyrene;

Methyl 3-{[2,6-dimethoxy-4-(2-phenylethoxy)benzyl]amino}-6-[4-(pyrrolidin-1-ylsulfonyl)phenyl]pyrazine-2-carboxylate polystyrene;

as a free base or a salt, solvate or solvate of a salt thereof.

25. A compound which is 4-{5-Amino-6-[(pyridin-3-ylamino)carbonyl]pyrazin-2-yl}benzoic acid as a free base or a salt, solvate or solvate of a salt thereof.

26. The use of the intermediates according to any one of claims 18 to 25 for the preparation of a compound of formula I as defined in claim 1.